

PATENT COOPERATION TREATY

PCT

COMMUNICATION OF
INTERNATIONAL APPLICATIONS

(PCT Article 20)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

Date of mailing:

28 November 1996 (28.11.96)

in its capacity as designated Office

The International Bureau transmits herewith copies of the international applications having the following international application numbers and international publication numbers:

International application no.:

PCT/US96/03649

International publication no.:

WO96/29413

**CORRECTED VERSION
VERSION CORRIGEE**The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer:

J. Zahra
Telephone No.: (41-22) 730.91.11

PATENT COOPERATION TREATY

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 05 November 1996 (05.11.96)	
International application No. PCT/US96/03649	Applicant's or agent's file reference PCT 19424Y
International filing date (day/month/year) 18 March 1996 (18.03.96)	Priority date (day/month/year) 22 March 1995 (22.03.95)
Applicant HOFMANN, Kathryn, J. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
08 August 1996 (08.08.96)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Marie-José Devillard Telephone No.: (41-22) 730.91.11
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PATENT COOPERATION TREATY

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NOTIFICATION CONCERNING
AMENDMENTS OF THE CLAIMS(PCT Rule 62 and
Administrative Instructions, Section 417)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as International Preliminary Examining Authority

Date of mailing:

05 November 1996 (05.11.96)

International application No.:

PCT/US96/03649

International filing date:

18 March 1996 (18.03.96)

Applicant:

MERCK & CO., INC. et al

The International Bureau hereby informs the International Preliminary Examining Authority that no amendments under Article 19 have been received by the International Bureau (Administrative Instructions, Section 417)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorised officer:

Marie-José Devillard

Telephone No.: (41-22) 730.91.11

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PCT 19424Y	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 96/03649	International filing date (day/month/year) 18/03/96	(Earliest) Priority Date (day/month/year) 22/03/95
Applicant MERCK & CO., INC. et al.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☒ Certain claims were found unsearchable (see Box I).

2. ☐ Unity of invention is lacking (see Box II).

3. ☒ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing

☐ filed with the international application.

☒ furnished by the applicant separately from the international application,

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the title, ☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is:

Figure No. _____ ☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 17,20
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 17,20 are directed to a method of treatment the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 96/03649

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/33 C07K14/025 C12N15/81 C07K16/08 A61K39/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO,A,94 20137 (UNIV ROCHESTER) 15 September 1994 see claims 1-40 ---	1-11
X	WO,A,94 00152 (UNIV GEORGETOWN) 6 January 1994 see claims 1-49 ---	1,3-11
X	EP,A,0 256 321 (BEHRINGWERKE AG) 24 February 1988 see claims 1-16 ---	1,3-11
X	EP,A,0 456 197 (BEHRINGWERKE AG) 13 November 1991 see claims 1-3 --- -/--	1,3-6

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

30 September 1996

Date of mailing of the international search report

22.10.96

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3016

Authorized officer

Gurdjian, D

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 96/03649

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	J MOL BIOL, FEB 20 1987, 193 (4) P599-608, ENGLAND, XP000603018 COLE ST ET AL: "Nucleotide sequence and comparative analysis of the human papillomavirus type 18 genome. Phylogeny of papillomaviruses and repeated structure of the E6 and E7 gene products." see the whole document ---	1-16,18, 19
Y	WO,A,94 05792 (US HEALTH) 17 March 1994 see page 10, paragraph 4; claims 1-46 ---	1-16,18, 19
A	WO,A,93 02184 (UNIV QUEENSLAND ;CLS LIMITED (AU)) 4 February 1993 see claims 1-64 -----	1-16,18, 19

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 96/03649

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9420137	15-09-94	AU-A- 6443694 EP-A- 0688227 JP-T- 8507685	26-09-94 27-12-95 20-08-96
WO-A-9400152	06-01-94	AU-A- 1135295 EP-A- 0647140	08-02-96 12-04-95
EP-A-0256321	24-02-88	DE-A- 3625257 AU-B- 597698 AU-A- 7601887 JP-A- 63214181	04-02-88 07-06-90 28-01-88 06-09-88
EP-A-0456197	13-11-91	DE-A- 4015044 AU-B- 650648 AU-A- 7621291 CA-A- 2042236 JP-A- 4227000	14-11-91 30-06-94 14-11-91 11-11-91 17-08-92
WO-A-9405792	17-03-94	US-A- 5437951 AU-A- 4847593 CA-A- 2143845 EP-A- 0662132 JP-T- 8504087	01-08-95 29-03-94 17-03-94 12-07-95 07-05-96
WO-A-9302184	04-02-93	AU-B- 651727 EP-A- 0595935 JP-T- 7505042	28-07-94 11-05-94 08-06-95

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

15
REC'D 04 JUL 1997

WIPO PCT

Applicant's or agent's file reference 19424Y-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US96/03649	International filing date (day/month/year) 18 MARCH 1996	Priority date (day/month/year) 22 MARCH 1995
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant MERCK & CO., INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of — sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 08 AUGUST 1996	Date of completion of this report 12 APRIL 1997
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer DAVID GUZO <i>David Guzo</i>
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US96/03649

I. Basis of the report

1. This report has been drawn on the basis of (*Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments*):

- ☒ the international application as originally filed.
- ☒ the description, pages 1-33 , as originally filed.
pages NONE , filed with the demand.
pages NONE , filed with the letter of _____.
pages _____ , filed with the letter of _____.
- ☒ the claims, Nos. 1-20 , as originally filed.
Nos. NONE , as amended under Article 19.
Nos. NONE , filed with the demand.
Nos. NONE , filed with the letter of _____.
Nos. _____ , filed with the letter of _____.
- ☒ the drawings, sheets/~~fig~~ 1-7 , as originally filed.
sheets/~~fig~~ NONE , filed with the demand.
sheets/~~fig~~ NONE , filed with the letter of _____.
sheets/~~fig~~ _____ , filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE .
- ☒ the claims, Nos. NONE .
- ☒ the drawings, sheets/~~fig~~ NONE .

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US96/03649

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. STATEMENT**

Novelty (N)

Claims 1-20 YESClaims NONE NO

Inventive Step (IS)

Claims 1-20 YESClaims NONE NO

Industrial Applicability (IA)

Claims 1-20 YESClaims NONE NO**2. CITATIONS AND EXPLANATIONS**

Claims 1-20 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed DNA, protein and antibody molecules. Also, the claimed vaccine compositions are not disclosed or suggested by the prior art and said vaccine compositions have industrial applicability as potential anti-papillomavirus infection treatments.

____ NEW CITATIONS ____

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US96/03649

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The description is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 5 because it fails to adequately enable practice of the claimed invention because:

Applicants claim a vaccine capable of preventing papillomavirus infection or a composition capable of inducing an immunological response to papillomavirus infection and uses thereof. The claims are not enabled however, because applicants have not demonstrated a composition capable of inducing a protective immune response in patients inoculated with said composition. Given that no human papillomavirus vaccines have been demonstrated prior to applicants invention, given that applicants present no data which would indicate to one of skill in the vaccine art that the instant compositions would be capable of acting as vaccines against papillomavirus infection, given that the vertebrate immune response is one of the most complex biological responses known and involves humoral, antibody and cell mediated immune responses, given the ability of human papillomaviruses to transform cells and evade host immunological responses, given that applicants have not disclosed how one would determine what constitutes an immunologically effective amount of the instant compositions, how often they would need to be administered, etc., it must be considered that applicants have not provided a disclosure sufficient to enable one of skill in the vaccine art to practice the claimed invention.

Claims 8-10, 15-17 and 20 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

Claim 1 is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claim is indefinite for the following reason(s): Applicants recite a DNA molecule which encodes human papillomavirus type 18. This is indefinite because it is unclear whether applicants mean to claim a DNA molecule encoding the entire genome of human papillomavirus 18 or some portion of the genome.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US96/03649

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

~~Sheet 10~~

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(6): A61K 39/12, 39/295; C12N 15/63, 15/64; C07K 14/005, 14/01, 14/025 and US Cl.: 424/204.1,
186.1; 435/69.1, 69.3, 320.1; 530/350; 536/23.72



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12N 15/37, C07K 14/025, 16/08, A61K 39/12		A2	(11) International Publication Number: WO 96/29413
			(43) International Publication Date: 26 September 1996 (26.09.96)
(21) International Application Number: PCT/US96/03649			(74) Common Representative: MERCK & CO., INC.; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).
(22) International Filing Date: 18 March 1996 (18.03.96)			
(30) Priority Data:			
08/408,669 22 March 1995 (22.03.95) US			
08/409,122 22 March 1995 (22.03.95) US			
(60) Parent Applications or Grants			(81) Designated States: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, <u>(US)</u> UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).
(63) Related by Continuation			
US 08/408,669 (CON)			
Filed on 22 March 1995 (22.03.95)			
US 08/409,122 (CON)			
Filed on 22 March 1995 (22.03.95)			
(71) Applicant (for all designated States except US): MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).			Published <i>Without international search report and to be republished upon receipt of that report.</i>
(72) Inventors; and			
(75) Inventors/Applicants (for US only): HOFMANN, Kathryn, J. [US/US]; (US). JANSEN, Kathrin, U. [DE/US]; (US). NEEPER, Michael, P. [US/US]; (US). JOYCE, Joseph, G. [US/US]; (US). GEORGE, Hugh, A. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).			
(54) Title: DNA ENCODING HUMAN PAPILLOMA VIRUS TYPE 18			
(57) Abstract The present invention is directed to DNA molecules encoding purified human papillomavirus type 18 and derivatives thereof.			